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Sir;

46/ Your note in NATURE brought back the days, some half century ago, of my time spent in Lederberg's lab on the Madison UW campus in '52-'54. The lab was small - in size and number of personnel - but he was already receiving numerous visitors, invited and appreciated or not. As I recall "Sir Mac" was among the former classification and I, as the only possessor of an auto (Josh hated to drive (thankfully) and Esther gave up an attempt to learn) was the "go-fer" to and from 'digs' and the airport. Josh and I were already acquainted: he being a med student at Columbia's med school and I a new grad student in the Zoo Dept (site of Thomas Hunt Morgan and the Fly Group for years); one at 158th St and the other at 116th St in Manhattan. He would come down to the lab to work with F. J. Ryan (later, my major prof) and we would dine on a hamburger and beer just before the 11 PM closing of the college beer hall: the Lions Den. With the war in Japan over he quit medical school and got into Yale through the good offices of F.J., who had post-docked with Beadle and Tatum (now respectively at Caltech and Yale) where his first discovery - sex in bacteria-- was made.

While there are many tales, and some probably true, at least in part, about Josh that float around, probably best left untold, I shall recount the home-made micromanipulator one.

Josh wanted to isolate the infrequent mating bacteria (as it was then thought to be - a sort of melding of the F+/Hfr and F- types - the F agent not having yet been discovered) and follow their progeny via micromanipulation. I, as a chemistry major, was assigned to find or synthesize another vital stain besides triphenyltetrazolium....used to count viable seeds at that time. Add bathochromic groups, said I. What are those?, asked Josh. Deepen color, shift absorbance spectrum: nitro groups are very good at that. Do it! Thus the F- strain could be stained pink and the F+/Hfr blue; quite appropriately. The relevant synthetischer papers were in Chemische Berichte '39-'44 by Brockman, and I blithely went ahead with appropriately derivatized nitroed reagents by standard procedures therefor. Fortunately I was working on a milligram scale, the reagents being costly and Josh's budget small, but I had advanced quant anal in college with A. A. Benedetti-Pichler, the Italian Austrian expatriate microanalyst (who developed and instructed Glenn Seaborg therein to purify the first plutonium during WW II). BOOM! No: a chemical one and not nuclear. Seems the nitrated triphenyl tets were being developed in Nazi Germany as primer compounds.

Josh, meanwhile, was making a micromanipulator; on an ingenuous concept of sliding plate glass squares, held together by highly viscous motor oil around a displaced pivot point joining them, thus reducing the motion of a long hand operated lever arm.

He did eventually acquire a Cailloux manipulator I think, and separated possible mating complexes via it, after another brain storm on enrichment: mating highly motile Hfr X fat 'couch-potato' non-motile bacteria: held in separate droplets but connected via a small tunnel - the 'males' would swim in, mate and then drag the attached female through another small tunnel into an empty chamber: catching them in flagrante delicto. He would then isolate the daughter cells as they were produced; 2, 4, 8, 16, 32.....until his hands flew like Liberace (the American pianist) playing the Minute Waltz in fifteen seconds.

There are many stories of Josh and Esther - "the Ladybirds" as they were known on the Madison campus - but many, most, are probably best left untold. He is almost forgotten there now, when I return (having retired from UWM).

In fact, at the August '97 "roast" (as we call them) held in honor of Wacław Szybalski's 75th birthday, the Sunday buffet lunch on the 'quadrangle' between the old Genetics Building (where he had his small lab) and the Institute of Biotechnology had a number of grad students therein in attendance (for the free beer, of course) and asked me, as an Old Boy, if I had been Wacław at <sup>with</sup> Madison. "No," I replied, "with Josh Lederberg, up there in the now Ag News Bldg on the 2nd floor - those two northeast windows were his lab and office." "Josh...Who?" they asked. Sic transit gloria.



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